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Case report

Two cases of a renal epithelial tumour resembling immature nephron

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Summary. Two cases of renal epithelial tumours are reported in females aged 46 and 66 years respectively. In spite of the large size of the tumours, neither invasive growth nor metastasis was observed. Histologically, the tumours were composed of immature epithelial cells forming tubules with abortive glomeruloid structures. Electron microscopy of tumour cells revealed poorly developed polarity and intracytoplasmic organelles. They showed similar immunohistochemical reactions to those of developing nephrons, particularly to those of the S-shaped body. The nuclear DNA content of the tumour cells was almost euploid. We conclude that the lesions were epithelial tumours of the kidney histologically mimicking developing renal parenchyma.

Key words: Renal neoplasia – Immature nephron – Glomeruloid bodies

Introduction

At present, the definition of renal epithelial tumours is still controversial. The World Health Organization (WHO) (Mostofi 1981) defines renal adenoma as the counterpart of renal cell carcinoma (RCC). In contrast, the Armed Forces Institute of Pathology (Bennington and Beckwith 1975) distinguishes between renal adenoma and RCC by their size. Thoenes et al. (1986) proposed a modification of the latter, applying nuclear grading.

In this paper, we present details of two renal epithelial tumours which are morphologically and immunohistochemically similar to immature nephrons with glomeruloid bodies. Such renal tumours have seldom been described. We consider them to be embryonal in nature, but to differ from the usual types of nephroblastoma.

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Case reports

Case 1. In July 1986, a 46-year-old Japanese housewife was admitted to Chigasaki Municipal Hospital complainting of abdominal fullness and gross haematuria. Her past and familial histories were not contributory. Radiological examination revealed a hypovascular tumour of the right kidney. Right nephrectomy with ureterectomy was performed on 5 August 1986 and postoperatively, the patient continues to do well (without chemotherapy).

The resected kidney contained a protruding tumour measuring 9 × 8 cm at the lower pole. It was sharply demarcated from the normal renal parenchyma without capsule formation, and was firm in consistency. The cut surface was homogeneous and milky white, without haemorrhage or calcification. There was no evidence of invasive growth or metastasis in the regional lymph nodes.

Case 2. In March 1986 a 66-year-old Japanese housewife was referred to Fujisawa Municipal Hospital with a complaint of persistent diarrhoea. Her past and familial histories were not contributory. The symptom was improved by medication, but a calcified tumour of the right kidney was noticed incidentally. Right nephrectomy was performed on 24 June 1986, and the patient is currently doing well 5 years after the operation.

The excised kidney contained a yellowish tumour measuring 8 cm in diameter at the lower pole. The tumour protruded from the cortex, and was well demarcated from the renal parenchyma. The cut surface of the tumour showed cystic degeneration. It was yellowish and hard in consistency with marked calcification. The cystic space was filled with coagulated blood. There was no evidence of invasive growth or metastasis.

Results

The histological features of the two tumours were similar (Fig. 1a). The margin between the renal parenchyma and tumour was very sharp, without capsule formation. There was no evidence of invasion of the adjacent tissue.

The tumour cells were uniform, small and cuboidal or flattened. They had large nuclei with coarse chroma-

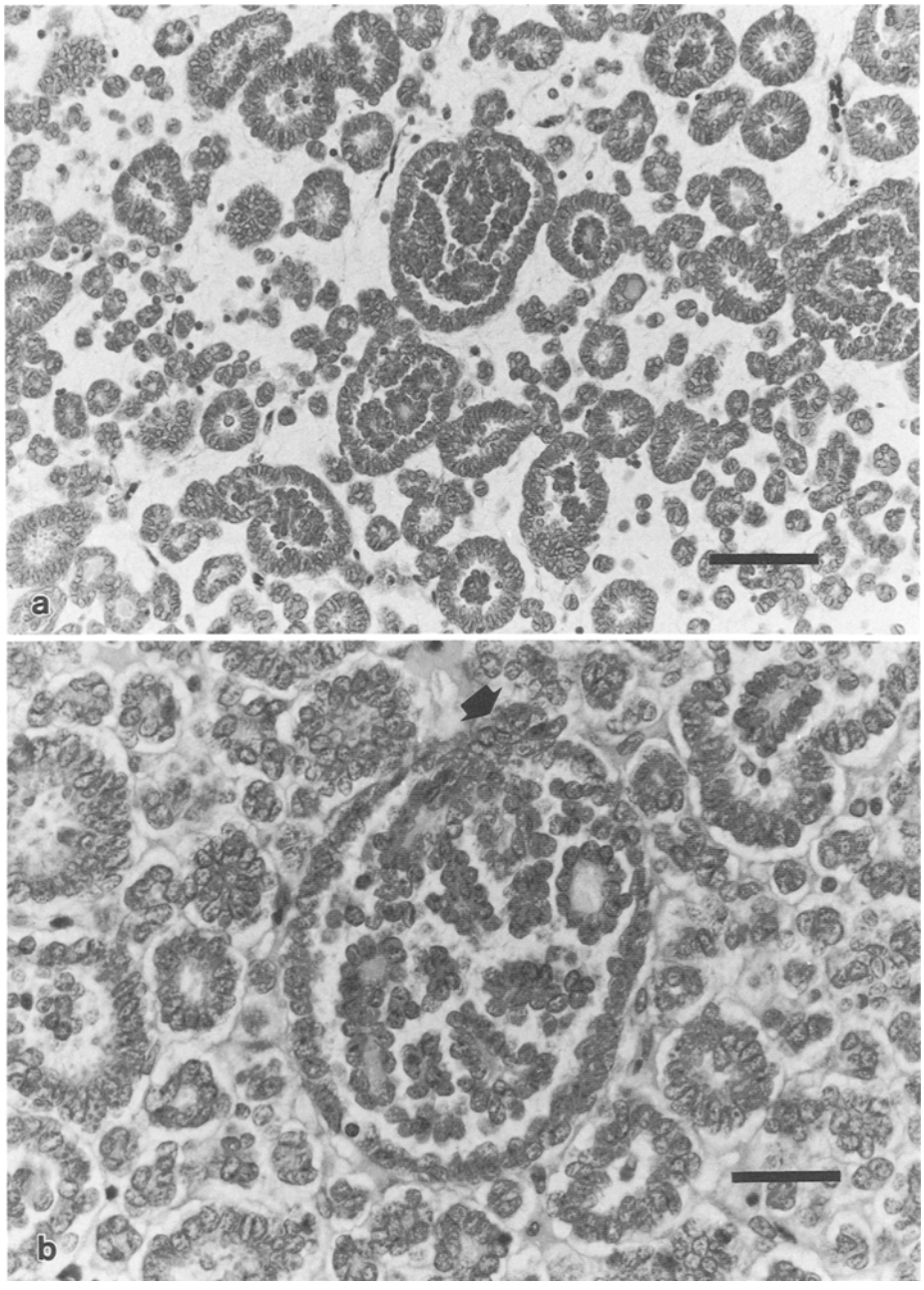

Fig. 1. a Histopathological findings of the present cases. Both tumours were composed of various-sized tubular structures. Note the glomeruloid bodies in the tumours. *Bar* represents 100 μm. **b** Higher magnification of the glomeruloid body. *Arrow* indicates the connection between the glomeruloid body and tubular structure, similar to normal glomeruli and tubules. *Bar* represents 25 μm

tin and very small nucleoli; the cytoplasm was scanty and slightly eosinophilic and no mitotic figures or bizarre giant cells were found. The cells formed cords and tubules. Focally, there were so-called glomeruloid bodies composed of lobulated papillary projections surrounded by capsules (Fig. 1 b). All of these structures had connection with tubular elements (Fig. 1 b, arrow). In the stalks of the projections, small amounts of acellular matrix were observed, but no capillary loops were identified. These structures were similar to the primitive glomeruli observed in the developing kidney (Ekblom 1981, 1985) and to the heterotopic glomerulogenesis reported in nephroblastoma (Payton et al. 1987). The stroma of each tumour was chiefly composed of oedematous or hyalinized tissue, with poor vascularization. In both cases, psammoma bodies were noted in the stroma and tubular lumina. In particular, case 2 showed remarkable stromal calcification with focal ossification. Methenamine silver and periodic acid-Schiff staining revealed basement membrane around the tubules and collagenous fibres in the tufts of the glomeruloid bodies.

For transmission electron microscopy, formalin-fixed tissue blocks were refixed with 3% glutaraldehyde and processed. Ultrastructurally, tumour cells forming tubular structures showed poorly developed polarity (Fig. 2). They had large round nucleoli and there were many free ribosomes and some rough endoplasmic reticulum with few mitochondria and lysosomes. The basal surface had accumulation of basal lamina matrix (arrowheads). The tubules had small-sized lumina associated

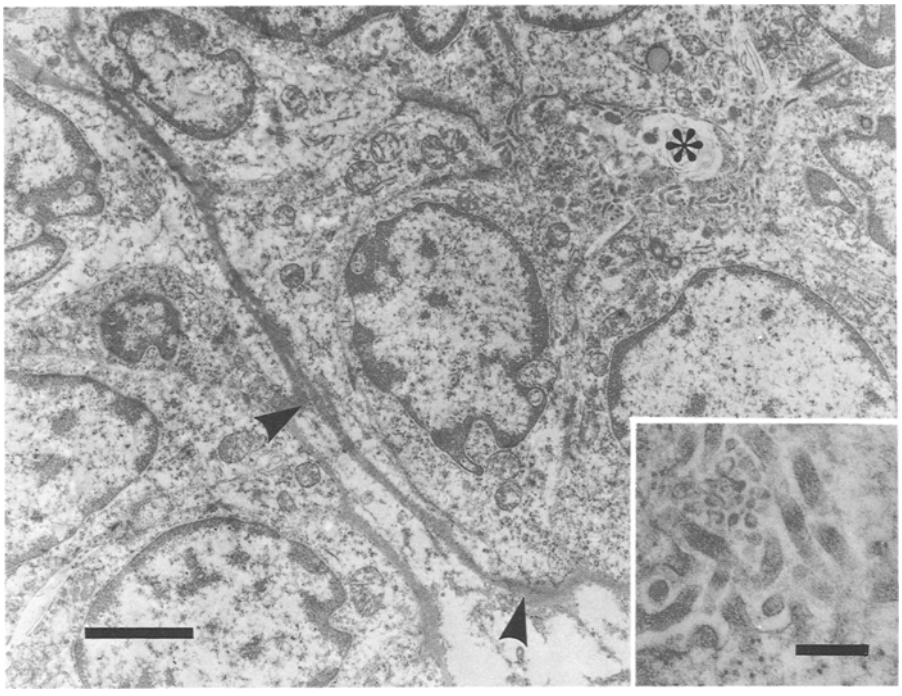

Fig. 2. Ultrastructural findings of the present cases. The tumour cells formed immature tubular structures with a narrow lumen (*asterisk*) and basal lamina (*arrowheads*). *Bar* represents 2 μm. *Inset:* There was a narrow luminal space associated with short microvilli. *Bar* represents 25 nm

with short microvilli (asterisk and inset). The papillary projections of glomeruloid structures were covered with flattened tumour cells and contained amorphous matrix in the stroma. There was no interaction with capillary loops. The capsules of the glomeruloid body had no microvilli on their apical surface (not shown).

Paraffin sections were used for immunohistochemistry and lectin histochemistry. The results of immunohistochemical staining of the tumours and of adult and embryonal kidneys are summarized in Table 1. Tumour cells forming tubules were positive for vimentin (Fig. 3a), Leu 7 (Fig. 3c; compare with Fig. 3d), S-100 protein (S-100) and S-100 α-subunit (S-100α) (Fig. 3e; compare with Fig. 3f) and, unexpectedly, negative for keratin (Fig. 3b) and epithelial membrane antigen (EMA). The tumour cells did not react with anti-Leu M1, lysozyme, α_1-antitrypsin (α_1AT), S-100 protein β subunit (S-100 β) and Tamm-Horsfall protein (THP) antibodies. Lectin histochemistry revealed that the apical surface of the tubules formed by tumour cells had positivity for *Arachis hypogaea* (peanut) agglutinin, but not for *Lotus tetragonolobus* agglutinin.

Spectrophotometric study was performed according to the method previously reported (Hamada and Fujita 1983), and showed that the majority of the tumour cells were euploid, and that a few cells were tetraploid.

Table 1. Results of immunohistochemical studies

Antibody or lectin	Reactivity of tumour cells	Portions showing positivity	
		In adult kidney	In fetal kidney
Keratin	Negative	DT, CD, PM	Cd
Vimentin	Positive	POD, PT, HL, DT	Blastema Immature tubules
Lysozyme	Negative	PT	None
α_1AT	Negative	PT	None
Leu 7	Positive	None	S-shaped body[a]
Leu M1	Negative	PT	None
THP	Negative	DT	None
EMA	Negative	DT, CD, PM	Mature tubules
S-100	Positive	PT, HL, DT, CD	Tubules[b]
S-100α	Positive	PT, CD	S-shaped body CD
S-100β	Negative	HL, DT, CD, PM	Tubules[b]
PNA	Positive	DT, CD, PM	Tubules[b]
LTA	Negative	PT, HL	Tubules[b]

α_1AT, α_1-Antitrypsin; THP, Tamm-Horsfall protein; EMA, epithelial membrane antigen; S-100, S-100 protein and its subunits; PNA, *Arachis hypogaea* agglutinin; LTA, *Lotus tetragonolobus* agglutinin; POD, podocyte; PT, proximal tubule; HL, Henle's loop; DT, distal tubule; CD, collecting duct; PM, pelvic mucosa

[a] Transiently expressed between 10th and 30th week of gestation

[b] Partially positive

Discussion

Histologically, these tumors were composed of immature cells forming both tubules and structures resembling the immature glomeruli of developing kidney. They seemed to have some resemblance to papillotubular RCCs. However, cellular atypia was not remarkable, and there was no invasive growth or metastasis in spite of the considerable tumour size. Furthermore, the glomeruloid structures were relatively uniform in size, and were connected to the tubular elements, as in normal glomeruli. Papillotubular RCCs would not show such a regular arrangement of tumour cells and it is difficult to consider the present tumours as examples of papillotubular RCCs.

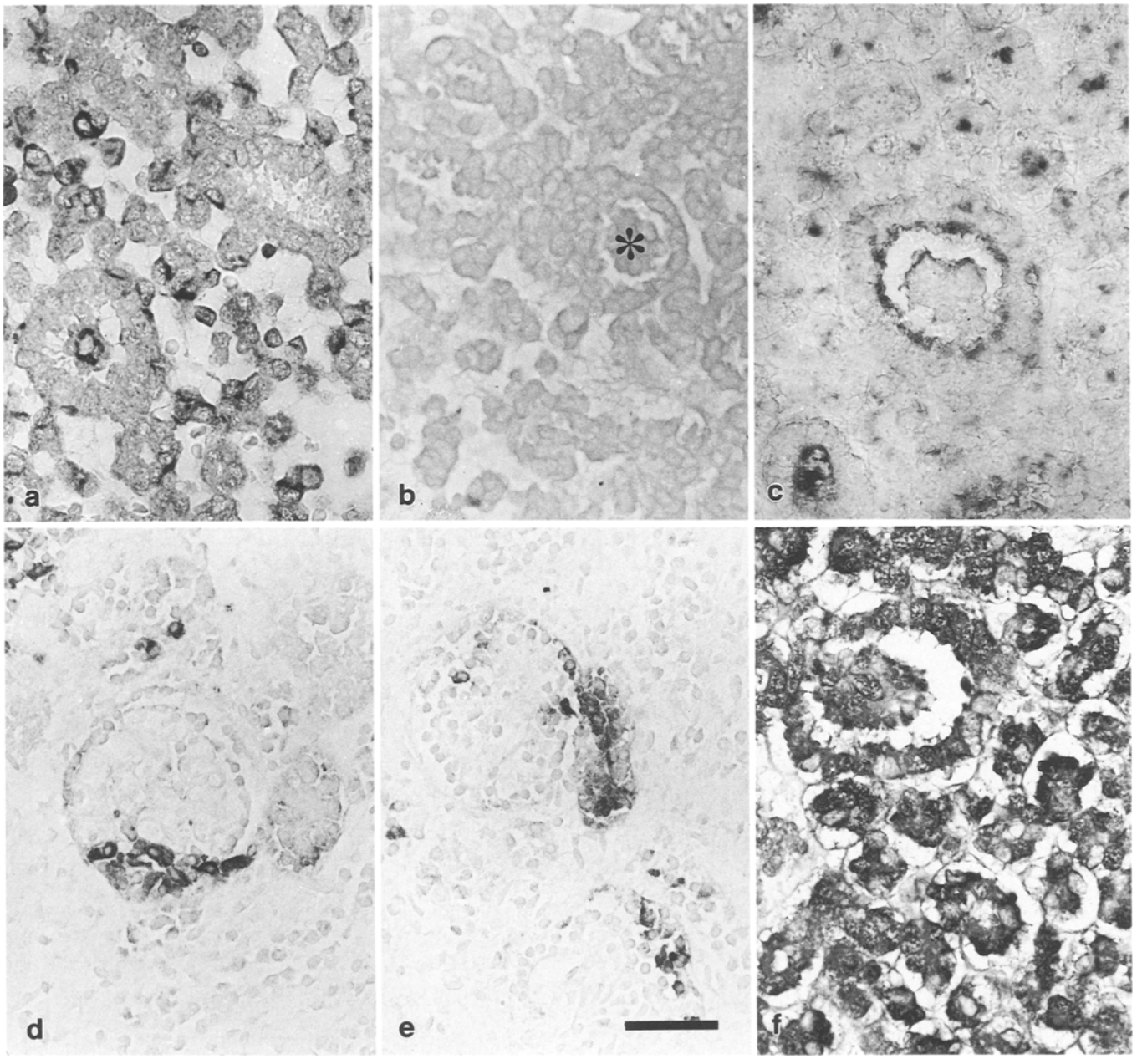

Fig. 3a–f. Immunohistochemical findings of the present tumours. Tumour cells were positive for vimentin (**a**), but not for keratin (**b**, *asterisk;* glomeruloid body). Leu 7 and S-100 protein α-subunit were positive both in the present tumour cells (**c** and **e**, respectively) and in the S-shaped body of the fetal kidney (**d** and **f**, respectively). *Bar* represents 50 μm

In order to determine their cellular origin, immunohistochemical examinations of the antigens expressed in various segments of the nephron were performed. It is known that keratin, EMA, α_1AT, lysozyme, THP and S-100 and its subunits are present in the segments of the nephron, and are widely used for examining the immunohistochemical characteristics of renal tumours in comparison with normal nephron segments (Wallance and Nairin 1971; Hoyer et al. 1974; Heyderman et al. 1979; van Dijk et al. 1979; Platt et al. 1983; Holthoefer et al. 1984; Fleming et al. 1985; Oosterwijk et al. 1986; Haimoto et al. 1987; Van Muijen et al. 1987; Cohen et al. 1988). Leucocytic surface antigens are also known to be expressed on the membrane of renal tubules (Borowitz et al. 1987; Platt et al. 1983). Leu M1, a surface glycoprotein of monocytes, has been reported to be expressed on the surface of proximal tubular epithelia, and is used for studying the histogenesis of RCCs (Hanjan et al. 1982). Leu 7 (Abo and Balch 1981), the other leucocyte surface antigen examined in this study, was positive on the cell membrane of the tumour cells and also on that of the epithelial cells of the S-shaped body of the fetal kidney. S-100 α was also positive (Fig. 3d, f). From our comparative immunohistochemical study using normal adult and fetal kidney tissues, the cellular origin of these lesions was not clearly determined, but the immunoreactivity pattern of the tumour cells was very similar to that of the S-shaped body in the fetal kidney. Similar studies have been performed on papillary RCC (Aizawa et al. 1987a, b; Wallance and Nairin

1971), and RCCs have been shown to have similar immunoreactivity to proximal or distal tubular epithelial cells, so that papillary RCCs are considered to be of lower nephron origin (Aizawa et al. 1987b). Therefore, the histogenesis of the present tumours as well as their morphological features seemed to be different from those of papillary RCCs.

Spectorphotometric analysis of nuclear DNA content has been used in the quantitative evaluation of the malignant potential of various tumours. From studies on RCCs, it has been clarified that the histological grade, nuclear DNA content and prognosis are correlated with each other, and that in low-grade RCCs, the tumour cells are predominantly euploid (Iwaya et al. 1987). Consequently, it is difficult to predict the biological behaviour of the present tumours.

Our cases showed some resemblance to nephroblastoma. Furthermore, immunohistochemical similarity to the S-shaped body has also been reported for sarcomatous nephroblastoma (Ishii et al. 1989). Nephroblastoma is rare in adulthood (Kilton et al. 1980; Kumar et al. 1984) and such cases are often difficult to distinguish from RCCs with sarcomatous change. Kilton et al. (1980) emphasized the necessity for a blastemal component in the diagnosis of nephroblastoma. Scharfenberg and Beckman (1985) reported a 54-year-old woman with a subcapsular renal nodular lesion composed of blastemal cells with abortive tubules and glomeruli, which the authors called persistent blastema. This lesion was histologically very similar to those in our cases, except for the presence of blastemal cells. The authors considered such a lesion to be a remnant of embryonal renal parenchyma and a possible precursor lesion of adult nephroblastoma. Because of the absence of blastemal tissue in our present cases, we do not consider them to be typical nephroblastoma or persistent blastema.

In summary, we have reported two cases of renal epithelial tumour similar to immature renal tissue. Although their exact biological behaviour was not established, these tumours should be distinguished from usual RCCs, adenomas and nephroblastomas.

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